U.S. DEPARTMENT OF COMMERCE
Patent and Trademark Office

13633

SEARCH REQUEST FORM

19723

Requestor's Name: DAVE NGUYEN JUL 21 2

Serial Number: 10/089,312

Date: 7/16/04 Phone: (STIC) 571-272-0931 Art Unit: 1652

2D31 2C18 1711

Search Topic:

Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevent citations, authors, keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevent claim(s).

Please search claim 21, wherein the zwitterionic phospholipid comprises $R^3COOCH_2CH(OCOR^4)CH_2OP(O)O^-$, which is linked to an alkanediyl- containing moiety; and wherein the cationic compound has the formula as set forth in claim 22.

Claim Sheet is attached !

2C2101

~~Specific species~~

Thanks

Dave Nguyen

Remsen 2D31

Mail Box 2C18

STAFF USE ONLY

Date completed: _____

Searcher: _____

Terminal time: _____

Elapsed time: _____

CPU time: _____

Total time: 1 30

Number of Searches: 48

Number of Databases: _____

Search Site

_____ STIC

_____ CM-1

_____ Pre-S

Type of Search

_____ N.A. Sequence

_____ A.A. Sequence

_____ Structure

_____ Bibliographic

Vendors

_____ IG

1068.94 STN

_____ Dialog

_____ APS

_____ Geninfo

_____ SDC

_____ DARC/Questel

_____ Other

PTO-1590 (9-90)

STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 127723

TO: Dave Nguyen **Location: rem/2d31/2c18** **Art Unit: 1632** **Thursday, July 29, 2004** **Case Serial Number: 10/089312**	**From: Paul Schulwitz** **Location: Biotech-Chem Library** **REM-1A65** **Phone: (571)272-2527** **paul.schulwitz@uspto.gov**

Search Notes

Examiner Nguyen,

See attached results.

If you have any questions about this search feel free to contact me at any time.

Thank you for using STIC search services!

Paul Schulwitz
Technical Information Specialist
STIC Biotech/Chem Library
(571)272-2527

STIC SEARCH RESUL FEEDBACK FORM

USPTO

Biotech-Chem Libra

Questions about the scope or the results of the search? Contact *the searcher or contact:*

Mary Hale, Information Branch Supervisor
571-272-2507 Remsen E01 D86

Voluntary Results Feedb

- *I am an examiner in Workgroup:* ☐ *Example: 1610*
- *Relevant prior art* **found**, *search results used as follows:*
  - ☐ 102 rejection
  - ☐ 103 rejection
  - ☐ Cited as being of interest.
  - ☐ Helped examiner better understand the invention.
  - ☐ Helped examiner better understand the state of the art in their technology.

  Types of relevant prior art found:
  - ☐ Foreign Patent(s)
  - ☐ Non-Patent Literature
    (journal articles, conference proceedings, new product announcements etc.)
- *Relevant prior art* **not found:**
  - ☐ Results verified the lack of relevant prior art (helped determine patentability)
  - ☐ Results were not useful in determining patentability or understanding the invention

Comments:

Drop off or send completed forms to STIC/Biotech-Chem Library Remsen Bldg.

SIRA
Search and Information Retrieval Administration

L5 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:265230 HCAPLUS
DOCUMENT NUMBER: 134:285563
ENTRY DATE: Entered STN: 13 Apr 2001
TITLE: Liposome-**entrapped** DNA **oral** vaccines
INVENTOR(S): **Gregoriadis, Gregory; Perrie, Yvonne**
PATENT ASSIGNEE(S): Lipoxen Limited, UK
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K009-127
SECONDARY: A61K048-00; C12N015-88
CLASSIFICATION: 63-3 (Pharmaceuticals)
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001024773	A1	20010412	WO 2000-GB3773	20001002
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1217989	A1	20020703	EP 2000-964471	20001002
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003529550	T2	20031007	JP 2001-527772	20001002

PRIORITY APPLN. INFO.: EP 1999-307786 A 19991001
WO 2000-GB3773 W 20001002
OTHER SOURCE(S): MARPAT 134:285563
ABSTRACT:
An oral vaccine comprises liposomes and complexed or, preferably, entrapped DNA operatively encoding an antigen, in which the liposomes are formed from components including cationic compds. and zwitterionic phospholipids. The hydrophobic groups within the liposome forming compds. must include at least one group which is saturated This is believed to raise the transition temperature, rendering the liposomes more stable when delivered orally. The compns. have been found to give detectable increased in IgA levels, secreted Igs of importance in efficacious oral vaccine delivery. Liposomes comprising phosphatidylcholine 32, dioleoyl phosphatidylethanolamine 16, and dioleoyl trimethylammonium propane 8 μmoles were prepared using the dehydration-rehydration method. PRc/CMV HBS plasmid DNA encoding for the small region of hepatitis B surface antigen was entrapped in the above liposome formulations. Entrapment complexation efficiency was 85-95%. Immunization of mice with the liposomes is described.

SUPPL. TERM: liposome phospholipid DNA oral vaccine
INDEX TERM: Lipids, biological studies

ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(glycerolipids; liposome-entrapped DNA oral vaccines)

INDEX TERM: Freeze drying
(liposome-entrapped DNA oral vaccines)

INDEX TERM: Antigens
DNA
Nucleic acids
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposome-entrapped DNA oral vaccines)

INDEX TERM: Phosphatidylcholines, biological studies
Polynucleotides
ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposome-entrapped DNA oral vaccines)

INDEX TERM: Drug delivery systems
(liposomes; liposome-entrapped DNA oral vaccines)

INDEX TERM: Vaccines
(oral; liposome-entrapped DNA oral vaccines)

INDEX TERM: Drying
(spray; liposome-entrapped DNA oral vaccines)

INDEX TERM: Phospholipids, biological studies
ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(zwitterionic; liposome-entrapped DNA oral vaccines)

INDEX TERM: 57-88-5, Cholesterol, biological studies 2462-63-7, Dioleoyl phosphatidylethanolamine 2644-64-6, Dipalmitoylphosphatidylcholine 4537-76-2, Distearoylphosphatidylethanolamine 4539-70-2, Distearoylphosphatidylcholine 5681-36-7, Dipalmitoylphosphatidylethanolamine 113669-21-9
ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liposome-entrapped DNA oral vaccines)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD.

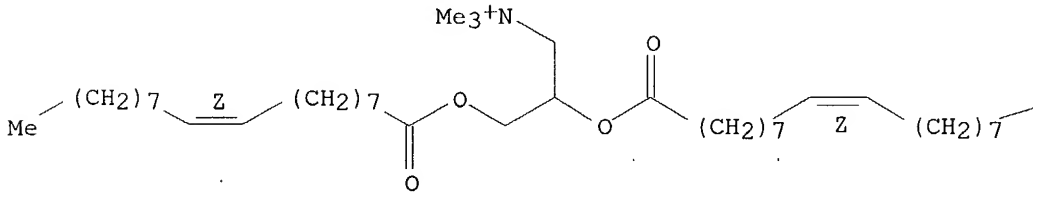
REFERENCE(S):

(1) Gregoriadis, G; WO 9810748 A 1998 HCAPLUS
(2) Gregoriadis, G; Febs Letters 1997, V402(2/03), P107
(3) Gregoriadis, G; Methods 1999, V19(1), P156 HCAPLUS
(4) Han, M; Journal of Veterinary Medical Science 1997, V59(12), P1109 HCAPLUS
(5) Perrie, Y; British Pharmaceutical Conference 1998, V50(Suppl), P103

L6 ANSWER 1 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN
RN **113669-21-9** REGISTRY
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[[(9Z)-1-oxo-9-octadecenyl]oxy]-(9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1-Propanaminium, N,N,N-trimethyl-2,3-bis[(1-oxo-9-octadecenyl)oxy]-, (Z,Z)-
FS STEREOSEARCH
MF C42 H80 N O4
CI COM
SR CA
LC STN Files: CA, CANCERLIT, CAPLUS, IPA, MEDLINE, PROMT, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Conference; Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation); PRP (Properties); USES (Uses)

Double bond geometry as shown.

PAGE 1-A



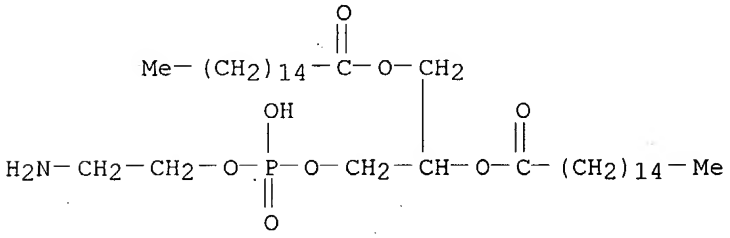
PAGE 1-B

Me

71 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
71 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L6 ANSWER 2 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN
RN **5681-36-7** REGISTRY
CN Hexadecanoic acid, 1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-ethanediyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:

CN Ethanol, 2-amino-, dihydrogen phosphate (ester), monoester with 1,2-dipalmitin, DL- (8CI)
CN Hexadecanoic acid, 1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-ethanediyl ester, (±)-
CN Palmitin, 1,2-di-, 2-aminoethyl hydrogen phosphate, DL- (8CI)
CN Palmitin, 1,2-di-, phosphate, 2-aminoethyl ester, dl- (6CI)
OTHER NAMES:
CN α-Cephalin, β,γ-dipalmitoyl-
CN β,γ-Dipalmitoyl-DL-α-cephalin
CN 1,2-Dipalmitoyl glycerylphosphorylethanolamine
CN 1,2-Dipalmitoyl-3-DL-glycerylphosphorylethanolamine
CN 1,2-Dipalmitoyl-DL-3-glycerophosphatidylethanolamine
CN 1,2-Dipalmitoyl-DL-phosphatidylethanolamine
CN 1,2-Dipalmitoyl-rac-glycerophosphoethanolamine
CN 1,2-Dipalmitoylphosphatidylethanolamine
CN Dipalmitoyl cephalin
CN Dipalmitoylphosphatidylethanolamine
CN DL-α-Cephalin dipalmitate
CN DL-α-Dipalmitoylphosphatidylethanolamine
CN DL-Dipalmitoylphosphatidylethanolamine
CN DPPE
FS 3D CONCORD
DR 3026-45-7
MF C37 H74 N O8 P
CI COM
LC STN Files: AGRICOLA, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CSCHEM, EMBASE, IPA, MEDLINE, PROMT, SPECINFO, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Conference; Journal; Patent; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1004 REFERENCES IN FILE CA (1907 TO DATE)
132 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1006 REFERENCES IN FILE CAPLUS (1907 TO DATE)
7 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L6 ANSWER 3 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN
RN **4539-70-2** REGISTRY
CN 3,5,9-Trioxa-4-phosphaheptacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxooctadecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Choline phosphate, 3-ester with 1,2-distearin (6CI)
CN Choline, hydroxide, dihydrogen phosphate, inner salt, ester with 1,2-distearin (8CI)
OTHER NAMES:
CN (±)-1,2-Distearoylglycero-3-phosphorylcholine
CN β,γ-Distearoylphosphatidylcholine
CN 1,2-Dioctadecanoyl-rac-glycerol-3-phosphorylcholine
CN 1,2-Distearoyl-3-glycerophosphorylcholine
CN 1,2-Distearoyl-DL-phosphatidylcholine
CN 1,2-Distearoylglycerol-3-phosphorylcholine
CN 1,2-Distearoylglyceryl 3-phosphorylcholine
CN 1,2-Distearoyllecithin
CN Coatsome MC 8080
CN Dioctadecanoyl phosphatidylcholine
CN Dioctadecanoyllecithin
CN Distearoyl-DL-α-phosphatidylcholine
CN Distearoyl-DL-phosphatidylcholine
CN Distearoyllecithin
CN Distearoylphosphatidylcholine
CN DL-α-Distearoyllecithin
CN DSPC
FS 3D CONCORD
DR 816-93-3, 159022-80-7, 107041-14-5, 201412-81-9
MF C44 H88 N O8 P
CI COM
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMCATS, CSCHEM, DDFU, DETHERM*, DRUGU, EMBASE, IPA, MEDLINE, PROMT, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Conference; Dissertation; Journal; Patent; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
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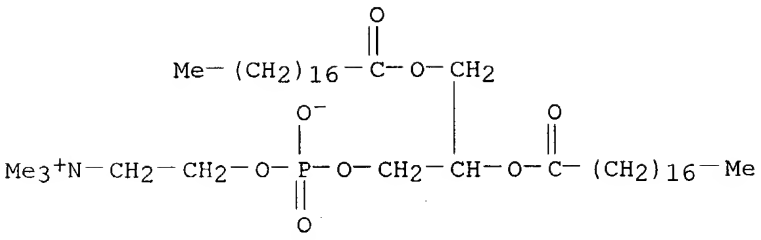

1372 REFERENCES IN FILE CA (1907 TO DATE)
22 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1374 REFERENCES IN FILE CAPLUS (1907 TO DATE)
2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L6 ANSWER 4 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN
RN **4537-76-2** REGISTRY
CN Octadecanoic acid, 1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-ethanediyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Ethanol, 2-amino-, dihydrogen phosphate (ester), monoester with 1,2-distearin, L- (8CI)
CN Stearin, 1,2-di-, 2-aminoethyl hydrogen phosphate (8CI)
CN Stearin, 1,2-di-, dihydrogen phosphate, 2-aminoethyl ester (7CI)
CN Stearin, 1,2-di-, phosphate, 2-aminoethyl ester (6CI)
OTHER NAMES:
CN 1,2-Dioctadecyl-rac-glycero-3-phosphoethanolamine
CN 1,2-Distearoyl phosphatidylethanolamine
CN 1,2-Distearoylglycerophosphorylethanolamine
CN Coatsome ME 8080
CN Distearoyl cephalin
CN Distearoyl-DL-α-phosphatidylethanolamine
CN Distearoylphosphatidylethanolamine
FS 3D CONCORD
DR 5683-47-6, 228086-93-9
MF C41 H82 N O8 P
CI COM
LC STN Files: ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMCATS, IPA, MEDLINE, PROMT, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Conference; Journal; Patent
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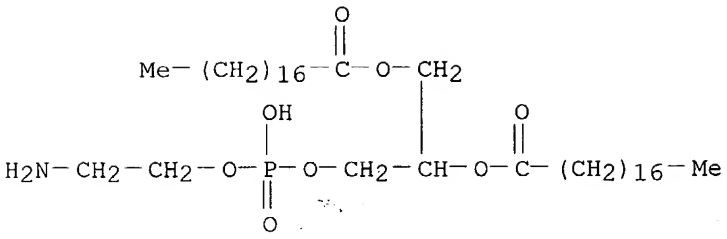

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

380 REFERENCES IN FILE CA (1907 TO DATE)
121 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
380 REFERENCES IN FILE CAPLUS (1907 TO DATE)
17 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L6 ANSWER 5 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN
RN **2644-64-6** REGISTRY
CN 3,5,9-Trioxa-4-phosphapentacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxohexadecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 3,5,9-Trioxa-4-phosphapentacosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxohexadecyl)oxy]-, hydroxide, inner salt, 4-oxide
CN Choline, hydroxide, dihydrogen phosphate, inner salt, ester with 1,2-dipalmitin (8CI)
CN Choline, phosphate, ester with 1,2-dipalmitin (6CI)
OTHER NAMES:
CN (±)-β,γ-Dipalmitoyl-α-lecithin
CN α,β-Dipalmitoylphosphatidylcholine
CN α-Glycerophosphorylcholine, β,γ-palmitoyl-
CN β,γ-Dipalmitoyl-DL-α-glycerylphosphorylcholine
CN β,γ-Dipalmitoyl-DL-α-lecithin
CN β,γ-Dipalmitoyl-DL-α-phosphatidylcholine
CN β,γ-Dipalmitoyl-DL-phosphatidylcholine
CN β,γ-Dipalmitoyllecithin
CN 1,2-Dihexadecanoyl phosphatidylcholine
CN 1,2-Dihexadecanoyl-rac-glycerol-3-phosphorylcholine
CN 1,2-Dipalmitoyl-α-phosphatidylcholine
CN 1,2-Dipalmitoyl-3-phosphatidyl choline
CN 1,2-Dipalmitoyl-3-phosphatidylcholine
CN 1,2-Dipalmitoyl-DL-α-phosphatidylcholine
CN 1,2-Dipalmitoyl-DL-phosphatidylcholine
CN 1,2-Dipalmitoylglycerol-3-phosphorylcholine
CN 1,2-Dipalmitoylglycerophosphorylcholine
CN 1,2-Dipalmitoyllecithin
CN 1,2-Dipalmitoylphosphatidylcholine
CN 1-Palmitoyl-2-palmitoylphosphatidylcholine
CN Coatsome MC 6060
CN Dihexadecanoyl phosphatidylcholine
CN Dipalmitoyl glycerophosphorylcholine
CN Dipalmitoyl-dl-α-lecithin
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CN Dipalmitoylglycerophosphocholine
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CN Dipalmitoylphosphocholine
CN DL-α-DPPC
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CN DL-β,γ-Dipalmitoyl-α-phosphatidylcholine
CN dl-1,2-Dipalmitoyl-3-phosphatidylcholine
CN DL-3-Dipalmitoylphosphatidylcholine
CN DL-Dipalmitoyl-α-lecithin
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CN DL-Dipalmitoylphosphatidylcholine
CN DPPC
CN DPPC (phosphatide)
CN rac-1,2-Dipalmitoylglycerol-3-phosphorylcholine
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LC STN Files: ADISNEWS, AGRICOLA, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, NIOSHTIC, PIRA, PROMT, SPECINFO, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Conference; Dissertation; Journal; Patent; Preprint; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
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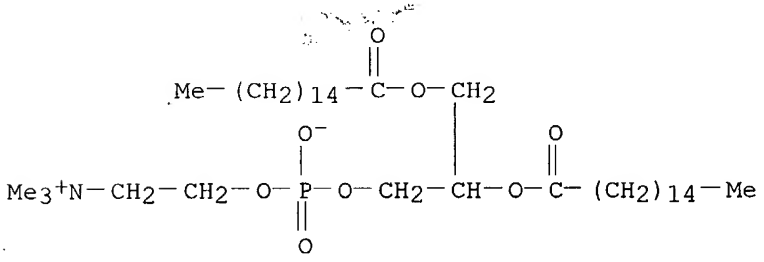
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent)

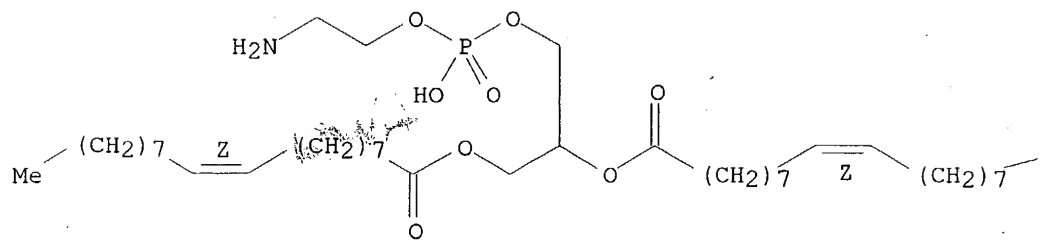


6032 REFERENCES IN FILE CA (1907 TO DATE)
69 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
6038 REFERENCES IN FILE CAPLUS (1907 TO DATE)
16 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L6 ANSWER 6 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN
RN **2462-63-7** REGISTRY
CN 9-Octadecenoic acid (9Z)-, 1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-ethanediyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 9-Octadecenoic acid (Z)-, 1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-ethanediyl ester
CN Ethanol, 2-amino-, dihydrogen phosphate (ester), monoester with 1,2-diolein (8CI)
CN Olein, 1,2-di-, 2-aminoethyl hydrogen phosphate (8CI)
CN Olein, 1,2-di-, dihydrogen phosphate, 2-aminoethyl ester (7CI)
CN Olein, 1,2-di-, phosphate, 2-aminoethyl ester (6CI)
OTHER NAMES:
CN 1,2-Dioleoyl phosphatidyl ethanolamine
CN Dioleoyl (glycerophospho)ethanolamine
CN Dioleoyl phosphatidylethanolamine
CN DL-Dioleoylphosphatidylethanolamine
CN DOPE
CN LipofectACE
FS STEREOSEARCH
DR 159317-98-3, 5683-54-5
MF C41 H78 N O8 P
CI COM
LC STN Files: AGRICOLA, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CSCHEM, EMBASE, IPA, MEDLINE, PROMT, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Conference; Dissertation; Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1125 REFERENCES IN FILE CA (1907 TO DATE)
52 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1129 REFERENCES IN FILE CAPLUS (1907 TO DATE)
19 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L6 ANSWER 7 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN
RN **57-88-5** REGISTRY
CN Cholest-5-en-3-ol (3β)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Cholesterol (8CI)
OTHER NAMES:
CN (-)-Cholesterol
CN Δ5-Cholesten-3β-ol
CN 3β-Hydroxycholest-5-ene
CN 5:6-Cholesten-3β-ol
CN Cholest-5-en-3β-ol
CN Cholesterin
CN Cholesteryl alcohol
CN Dythol
CN Lidinit
CN Lidinite
CN NSC 8798
CN Provitamin D
FS STEREOSEARCH
DR 80356-33-8, 209124-38-9, 218965-24-3, 262418-13-3, 378185-03-6, 676322-57-9
MF C27 H46 O
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES, DIPPR*, DRUGU, EMBASE, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT,

IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PDLCOM*, PIRA, PROMT, RTECS*, SPECINFO, TOXCENTER, TULSA, ULIDAT, USAN, USPAT2, USPATFULL, VETU, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

DT.CA CAplus document type: Book; Conference; Dissertation; Journal; Patent; Preprint; Report

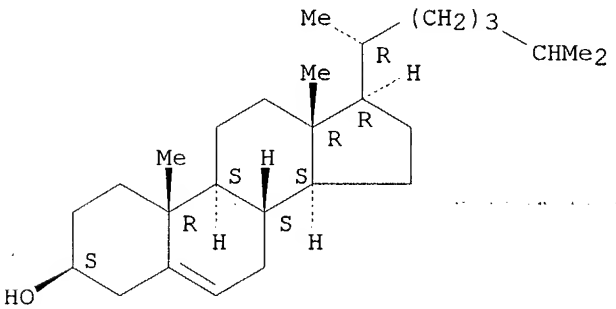
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); CMBI (Combinatorial study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)

RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)

RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

104023 REFERENCES IN FILE CA (1907 TO DATE)
8887 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
104207 REFERENCES IN FILE CAPLUS (1907 TO DATE)
15 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

$R^1OCH_2CH(OR^2)CH_2$

linked to a moiety made of groups to which the species requirement has been applied.

Since all of the alternatives possess a common significant structural element and all of the combinations have the same utility, it is respectfully submitted that unity is present. Withdrawal of the species requirement is therefore respectfully solicited.

In an attempt to be complete, applicants advise the Examiner as follows. With respect to species requirement 1, applicants select the species where Y is O, and for species requirement 2, applicants select the species where X^2 is N or P when m is 3; if a requirement is made to select within this group, applicants select nitrogen. With respect to the species requirement 3, of the species of R^8 listed in claim 21 applicants select C_{1-8} alkyl. In response to species group 4, applicants select R^5 being a bond, and with regard to the species group designated 5, applicants select the species where X^1 is N or P when n is 3, and if required to select further, applicants would select nitrogen. As to species group 6, of the species of R^6 listed in claim 22, applicant select C_{1-8} alkyl. Finally, with regard to species group 7, applicants select the first listed species in claim 32, namely distearoylphophatidylcholine.

Applicants believe that all of the instant claims read on the elected species, however defined, other than claims 33 and 48.

the Patent Office is authorized to charge the underpayment to Deposit Account No. 04-1073.

AMENDMENTS

In the Claims:

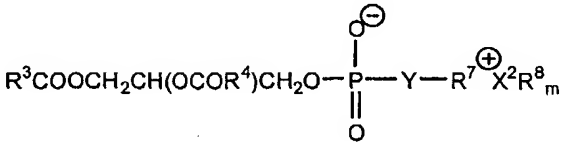
Please cancel claim 1 without prejudice.

Please add new claims 21-49 pursuant to 37 C.F.R. § 1.121(c)(1)(i) as set forth in the "clean" version set forth below. Entry is respectfully requested.

21(NEW). An oral vaccine comprising a nucleic acid operatively encoding an antigen complexed with or entrapped within liposomes formed from liposome forming components and comprising

a) at least one cationic compound;

b) zwitterionic phospholipid consisting of one or two compounds having the general formula II



II

in which R^3 and R^4 are the same or different and are a group of the formula $CH_3(CH_2)_e(CH{=}CH\text{-}CH_2)_f(CH_2)_g$- in which f is 0 to 6, each of e and g are 0 to 23 and e + g and 3f is in the range 12 to 23;

R^7 is a $C_{1\text{-}8}$ alkanediyl group;

Y is -O- or a bond;

X^2 is N, P or S;

m is 3 when X^2 is N or P and is 2 when X^2 is S; and

the groups R^8 are the same or different and are selected from the group consisting of hydrogen, C_{1-8} alkyl, C_{6-11} aryl or aralkyl, or two or three of the groups R^8 together with X^2 form a saturated or unsaturated heterocyclic group having 5 to 7 ring atoms,

in which at least 50% by mole of groups R^3 and R^4 has a value for f of 0 and which comprises a compound in which R^3 and R^4 are the same and have a value for f of 0:

in which the molar ratio of cationic compound to zwitterionic phospholipid is in the range of 1:1 to 1:10.

22(NEW). A vaccine according to claim 21 in which the cationic compound has the general formula I,

$$R^1OCH_2CH(OR^2)CH_2R^5X^1R^6_n \qquad I$$

in which R^1 and R^2 are the same or different and are a group of the formula $CH_3(CH_2)_a(CH{=}CH\text{-}CH_2)_b(CH_2)_c(CO)_d$- in which b is 0 to 6, a and c are each selected from 0-23 and (a + c + 3b) is in the range 12-23 and d is 0 or 1;

R^5 is a bond or a C_{1-8} alkanediyl group;

X^1 is N, P or S;

n is 3 where X^1 is N or P and is 2 where X^1 is S; and

the groups R^6 are the same or different and are selected from the group consisting of hydrogen, C_{1-8} alkyl, C_{6-12} aryl and aralkyl, or two or three of the groups R^6 together with X^1 form a saturated or unsaturated heterocyclic group having 5 to 7 ring atoms.

23(NEW). A vaccine according to claim 22 in which R^1 is the same as R^2 and R^3 is the same as R^4.

24(NEW). A vaccine according to claim 23 in which R^1 and R^2 represent a different group to R^3 and R^4.

25(NEW). A vaccine according to claim 23 in which R^1 and R^2 represent a different group to R^3 and R^4 , and in which in R^1 and R^2, b is 1, and in which (a + c) is in

the range 10 to 20.

26(NEW). A vaccine according to claim 23 in which d is 0.

27(NEW). A vaccine according to claim 22 in which X^1 is N and in which the R^6 groups are all C_{1-4} alkyl.

28(NEW). A vaccine according to claim 21 which comprises two zwitterionic phospholipids in each of which Y is O, X^2 is N, and the groups R^8 of the first phospholipid are all hydrogen and the groups R^8 of the second phospholipid are all C_{1-4} alkyl.

29(NEW). A vaccine according to claim 28 in which, in each phospholipid R^7 is $(CH_2)_h$ in which h is 2 or 3.

30(NEW). A vaccine according to claim 28 in which the groups R^3 and R^4 of the said first phospholipid are the same and each is a group in which f is1 and (e + g) is in the range 10 to 20.

31(NEW). A vaccine according to claim 30 in which in the groups R^3 and R^4 of the said second phospholipid are the same, f is O and e + g is in the range 15 to 23.

32(NEW). A vaccine according to claim 31 in which the said second zwitterionic phospholipid is selected from the group consisting of distearoylphosphatidylcholine, distearoylphosphatidylethanolamine, diplamitoylphosphatidylcholine and dipalmitoylphosphatidylethanolamine.

33(NEW). A vaccine according to claim 21 in which the cationic compound is cholesterol-3β-N-(dimethyaminoethyl) carbamate.

34(NEW). An oral vaccine according to claim 21 in which the liposome forming components include at least 25 mole% of components which individually have a transition temperature of more than 40°C.

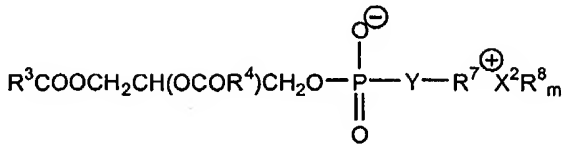
35(NEW). A vaccine according to claim 21 in which the nucleic acid is entrapped within the liposomes.

36(NEW). A method of entrapping polynucleotide into liposomes involving the steps of:

i) forming an aqueous suspension comprising naked nucleic acid, which operatively encodes an immunogenic polypeptide useful to induce a desired immune response in a human or animal subject, and preformed liposomes formed of liposome forming components comprising

a) at least one cationic compound;

b) zwitterionic phospholipid consisting of one or two compounds having the general formula II



II

in which R^3 and R^4 are the same or different and are selected from groups of the formula $CH_3(CH_2)_e(CH{=}CH\text{-}CH_2)_f(CH_2)_g$- in which f is 0 to 6, each of e and g are 0 to 23 and e + g and 3f is in the range 12 to 23;

R^7 is a $C_{1\text{-}8}$ alkanediyl group;

Y is -O- or a bond;

X^2 is N, P or S;

m is 3 when X^2 is N or P and is 2 when X^2 is S; and

the groups R^8 are the same or different and are selected from the group consisting of hydrogen, $C_{1\text{-}8}$ alkyl, $C_{6\text{-}11}$ aryl or aralkyl, or two or three of the groups R^8 together with X^2

form a saturated or unsaturated heterocyclic group having 5 to 7 ring atoms,

in which at least 50% by mole of groups R^3 and R^4 has a value for f of 0 and which comprises a compound in which R^3 and R^4 are the same and have a value for f of 0:

in which the molar ratio of cationic compound to zwitterionic phospholipid is in the range of 1:1 to 1:10.

ii) freeze-drying or spray-drying the suspension, and

iii) rehydrating the product of step ii) to form dehydration/rehydration vesicles.

37(NEW). A method according to claim 36 comprising the further steps of:

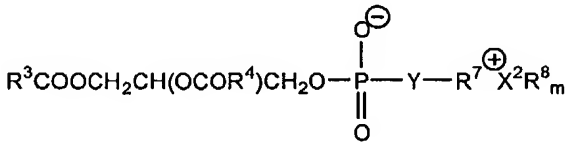
iv) subjecting the aqueous suspension of dehydration/rehydration vesicles from step iii to microfluidization to control their size; and

v) optionally separating non-entrapped nucleic acid from liposomes.

38(NEW). Method of vaccinating an animal comprising administering orally a composition comprising a nucleic acid operatively encoding an antigen complexed with or entrapped within liposomes formed from liposome forming components comprising

a) at least one cationic compound

b) zwitterionic phospholipid consisting of one or two compounds having the general formula II



II

in which R^3 and R^4 are the same or different and are a group of the formula $CH_3(CH_2)_e(CH{=}CH\text{-}CH_2)_g$- in which f is 0 to 6, each of e and g + 3f are 0 to 23 and e + g is in the range 12 to 23;

R^7 is a $C_{1\text{-}8}$ alkanediyl group;

Y is -O- or a bond;

X^2 is N, P or S;

m is 3 when X^2 is N or P and is 2 when X^2 is S; and

the groups R^8 are the same or different and are selected from the group consisting of hydrogen, C_{1-8} alkyl, C_{6-11} aryl or aralkyl, or two or three of the groups R^8 together with X^2 form a saturated or unsaturated heterocyclic group having 5 to 7 ring atoms;

in which at least 50% by mole of groups R^3 and R^4 has a value for f of 0 and which comprises a compound in which R^3 and R^4 are the same and have a value for f of 0,

wherein the molar ratio of cationic compound to zwitterionic phospholipid is in the range 1:1 to 1:10,

whereby an immune response to the said antigen is generated.

40(NEW). A method according to claim 38 in which the cationic compound has the general formula I,

$$R^1OCH_2CH(OR^2)CH_2R^5X^1R^6_n \qquad I$$

in which R^1 and R^2 are the same or different and are a group of the formula $CH_3(CH_2)_a(CH{=}CH\text{-}CH_2)_b(CH_2)_c(CO)_d$- in which b is 0 to 6, a and c are each selected from 0-23 and (a + c + 3b) is in the range 12-23 and d is 0 or 1;

R^5 is a bond or a C_{1-8} alkanediyl group;

X^1 is N, P or S;

n is 3 where X^1 is N or P and is 2 where X^1 is S; and

the groups R^6 are the same or different and are selected from the group consisting of hydrogen, C_{1-8} alkyl, C_{6-12} aryl and aralkyl, or two or three of the groups R^6 together with X^1 form a saturated or unsaturated heterocyclic group having 5 to 7 ring atoms.

41(NEW). A method according to claim 40 in which R^1 is the same as R^2 and R^3 is the same as R^4.

42(NEW). A method according to claim 41 in which R^1 and R^2 represent a

different group to R^3 and R^4.

43(NEW). A method according to claim 41 in which R^1 and R^2 represent a different group to R^3 and R^4, in which in R^1 and R^2, b is 1, and in which (a + c) is in the range 10 to 20.

44(NEW). A method according to claim 38 in which the liposome forming materials comprise two zwitterionic phospholipids in each of which Y is O, X^2 is N, and the groups R^8 of the first phospholipid are all hydrogen and the groups R^8 of the second phospholipid are all C_{1-14} alkyl, and R^7 is $(CH_2)_h$ in which h is 2 or 3.

45(NEW). A method according to claim 44 in which the groups R^3 and R^4 of the said first phospholipid are the same and each is a group in which f is 1 and (e + g) is in the range 10 to 20.

46(NEW). A method according to claim 45 in which in the groups R^3 and R^4 of the said second phospholipid are the same f is 0 and e+ g is in the range 15 to 23.

47(NEW). A method according to claim 46 in which the said second zwitterionic phospholipid is selected from the group consisting of distearoylphosphatidylcholine, distearoylphosphatidylethanolamine, diplamitoylphosphatidylcholine and dipalmitoylphosphatidylethanolamine.

48(NEW). A method according to claim 38 in which the cationic compound is cholesterol-3β-N-(dimethyaminoethyl) carbamate.

49(NEW). A method according to claim 38 in which the nucleic acid is entrapped within the liposomes.